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Is passive smoking an added risk factor for lung cancer in Chinese women?

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200 female lung cancer patients and 200 healthy district controls were interviewed to identify and quantify the various sources of passive smoking among Chinese females in Hong Kong. For the ever-smokers, passive exposure from external sources did not appear to add to their risk. For the never-smokers, qualitative assessments (smoke exposure categories, age when passive exposure started), and quantitative assessments (hours, years, intensity) showed no significant differences between the data for patients and controls. Moreover, higher relative risks were not associated with higher levels of passive smoking for the ever or never-smokers. Thus, our findings would seem to indicate that passive smoking, as an isolated factor, did not have an influence on female lung cancer incidence in Hong Kong.

Recently, there has been renewed discussion on the possible effects of passive smoking on lung cancer risk (5, 8, 19). In previous studies on the possibility of increased risk of lung cancer among wives/husbands from their smoking spouses, the data (2, 9, 12, 16) were only based on whether the spouse smoked (yes/no) with no further qualifications on whether the smoker actually smoked in the presence of the subject and for how long.

Where « quantification » was done (5, 17, 18), it was based on the current spouse's smoking habits. It is well known that the carcinogenetic process of internal solid cancers usually begins 20 or more years before diagnosis when there might have been no exposure from the current source. Furthermore, little account was taken of changes in smoking habits or marriage, or the possibility of exposure from the work environment. Some of these problems were raised by Hammond and Selikoff (11) but they have yet to be addressed by epidemiological studies to date.

Chinese females in Hong Kong have an average annual age-standardized incidence rate of 24.1/100,000 for lung cancer (13). This is among the highest rates for women in the world. In order to more directly assess the possible role of passive smoking in lung cancer development, a retrospective study of 200 female lung cancer patients and 200 healthy district controls was begun in 1981. Hong Kong, with an average urban density of 28,000 inhabitants per square kilometer, and 8 m^2 of average living space per person, is one of the most densely populated areas in the world. It is, therefore, an appropriate place to test the passive smoking aetiological hypothesis.

Patients and methods

The 200 lung cancer patients studied were from the wards or out-patient departments of 8 hospitals

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in Hong Kong. Patients were interviewed as they became available. Eight possible subjects were not interviewed because they were not sufficiently alert to answer our questions. Another 18 had to be excluded after interviews had been completed, when later evidence and checking revealed that their lung tumours were secondaries and not primaries. Medical records and radiographs were reviewed by J.H.-C.H., and pathology specimens were verified by D.S. with her colleagues. Where necessary, additional diagnostic procedures were requested to complete the data.

Patients were matched with an equal number of healthy controls by age stratification (± 5 years) in each district (n = 34), and by socio-economic status. Controls were interviewed at their homes within a few weeks after their matched patients had been identified.

Two female research assistants, fluent in Chinese and English, conducted the interviews using a tape recorder and semi-structured questionnaire. Utilizing interview techniques from the social sciences, especially those related to the gathering of life histories, the interviewers were trained to probe for details and elaboration of facts. Data were obtained on the changes in residence patterns since birth (where lived, how long, how many together, what type of housing, how many rooms); occupational history (where worked, what done, level of pollution, how long); active smoking (type of tobacco, method of smoking, and amount currently smoked and at 10, 20, 30, 40, 50 or more years ago, and inhalation practices); passive smoking (from whom, what type of tobacco product, amount they probably smoked per day, amount of time of exposure, when stopped or changed); personal and family histories (age at marriage, divorce, separation, and/or widowhood; number of children, occupations of parents and spouse); etc. The taped interviews were transcribed and then checked by L.C.K. for points that had been left out, or for inconsistencies, e.g. comparing passive smoking exposures with residential and marriage histories. Where necessary, subjects were recontacted for further information. The mean age of the patients was 61.8 years (S.D. 10.0) and that for the controls was 60.6 years (S.D. 9.6).

Results

Histological distribution

The histological distribution according to WHO 2nd Edition (20) and basis of diagnosis of the patients are shown in Table I.

The predominant cell type was adenocarcinoma, forming 34.5% of the total sample, or 38% of those with histological typing. However, when the frequencies of squamous plus small cell types are compared with adenocarcinoma plus large cells, the resulting, Kryberg ratio (6) of 1.16 still showed a preponderance of the former group of tumours. This low relative frequency of adenocarcinomas in Hong Kong Chinese females was also found by Chan and MacLennan (3).

Smoke exposure categories

From our interviews, three major regular sources of tobacco smoke were identi-

Table I - *Cell type and basis of diagnosis.*

	Cell type							
	Squamous No. (%)	Small cell No. (%)	Adeno-carcinoma No. (%)	Large cell No. (%)	Mixed No. (%)	Carcinoid No. (%)	Unclassified No. (%)	Total No. (%)
Bronchoscopic biopsy*	26 (13.0)	14 (7.0)	9 (4.5)	4 (2.0)	3 (1.5)	-	9 (4.5)	65 (32.5)
Resection	14 (7.0)	7 (3.5)	33 (16.5)	3 (1.5)	3 (1.5)	1 (0.5)	1 (0.5)	62 (31.0)
Lymph node	9 (4.5)	4 (2.0)	10 (5.0)	2 (1.0)	-	-	-	25 (12.5)
Pleural	-	1 (0.5)	5 (2.5)	2 (1.0)	-	-	1 (0.5)	9 (4.5)
Sputum cytology	7 (3.5)	11 (5.5)	12 (6.0)	-	1 (0.5)	-	1 (0.5)	32 (16.0)
Radiological & clinical	-	-	-	-	-	-	7 (3.5)	7 (3.5)
Total	56 (28.0)	37 (18.5)	69 (34.5)	11 (5.5)	7 (3.5)	1 (0.5)	19 (9.5)	200 (100)

* *Includes transbronchial biopsy.*

fied. In addition to ever-smokers (S), there were those who had cohabiting relatives smoking in their presence at home (H), or those daily exposed at their workplace for a number of years (W). In Fig. 1 three intersecting circles have been drawn to shown seven possible categories and one isolated circle (N) representing those who had never been exposed to any of these regular sources. Passive exposure is denoted by the shaded area, and includes sidestream smoke from home or workplace.

To see whether this qualitative method of assessment would discriminate higher risk groups, all patients and controls were fitted into each of these 8 different smoke exposure categories and the odds ratios were calculated (Table II). If those claiming none (N) represent the standard with a relative risk (RR) of 1.00, smokers with no other source of exposure (S) or multiple sources (SH, SW, SHW) had RRs ranging from 2.56 to 5.45, whereas non-smokers who were only exposed to passive smoking at home (H), workplace (W), or both (HW) had RRs only marginally

Table II - *Relative risks (RR) for different exposure categories.*

A. Single categories

Exposure category	Patients	Controls	RR
S	33	11	5.45
H	57	85	1.22
W	2	4	0.91
SH	62	44	2.56
SW	2	1	3.64
HW	7	8	1.59
SHW	15	7	3.90
N	22	40	1.00
Total	200	200	

B. Categories combined

Exposure category	Patients	Controls	RR
S + SH + SW + SHW	112	63	3.23*
H + W + HW	66	97	1.24*
N	22	40	1.00
Total	200	200	

* $p \leq 0.00001$ $p \leq 0.44$

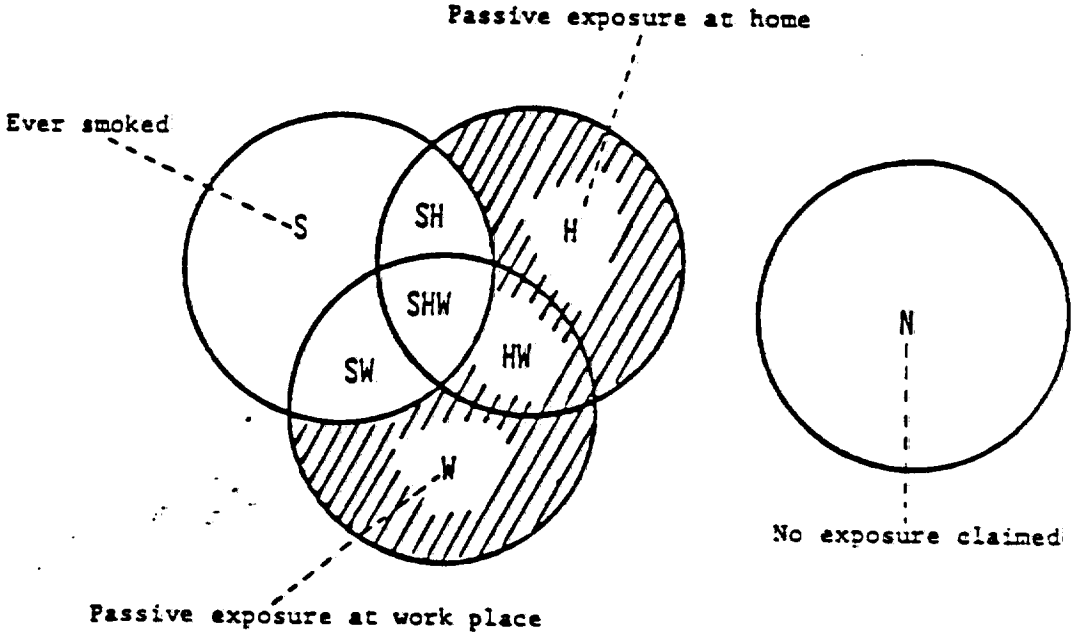

Fig. 1 - *Smoke exposure categories.*

greater than 1.00 (range 0.91-1.59). When smokers and those only passively exposed were grouped (Table IIB), the RR of active smokers was 3.23, and that for the passive smokers a non-significant 1.24.

Quantification of passive smoking

Our detailed interviews allowed us to estimate the amounts of passive smoking from various places in terms of hours or years (Table III). Smokers as a group had more exposure to passive smoking from others than the never-smokers. Depending on the unit of measurement, whether hours or years, we found that among the smokers, the patients had more hours of exposure, but the controls had more years. Among the never-smokers, the controls actually had more hours or years than the patients, but these differences were minimal. Hours per year was used as a measure of intensity of passive exposure. Overall, there was no significant difference in exposure levels between patients and controls, whether they were smokers or never-smokers.

Table III - *Average accumulative passive tobacco smoke exposure by place.*

Place	Per smoker*		Per never-smoker	
	79 patients	52 controls	66 patients	97 controls
I. Home				
Hours	22,773	21,517	15,789	18,926
Years	28.7	31.5	25.7	25.8
II. Workplace				
Hours	6,352	1,867	2,121	1,681
Years	3.8	1.7	2.0	1.2
III. Total amounts				
Hours	28,703	23,385	17,582	20,957
Years	30.0	32.6	26.4	26.3
Hours/year	956.8	717.3	677.3	762.6

* *Excluded were 33 patients and 11 controls without passive exposure.*

Since about 90% of the total amounts of passive smoking came from the home. Table IV shows the average contribution from each cohabiting relative who smoked in the presence of the subject. Only direct exposure was counted. Husbands who smoked, but did not expose their wives to passive smoking for various reasons, such as living overseas, on travelling jobs, etc., were not included in the estimations. From the Chinese cultural practice of having extended family members living together, the female could be exposed to her parents' cigarettes or pipe when young, to her husband's and in-laws' tobacco during marital life, and to her children's cigarettes when old. Although in terms of hours/person, parents were found to be a heavy source of sidestream smoke, only a minority of patients or controls were so exposed. The most frequent source was that from the husband.

About 2/3 of the total hours of tobacco exposure were calculated from our data to be from the husband's cigarettes. Both cases and controls had an average of about 20,000 hours of passive smoking from their homes, so that no significant difference in exposure levels was found between them.

Table IV - *Source of passive exposure at home.*

	Average total amounts			
	141 patients		144 controls	
	No.	Hours/person	No.	Hours/person
Husband	115	18,183	111	19,314
Parents	18	27,994	21	27,748
In-laws	7	28,257	8	9,175
Children	24	3,804	33	4,170
Others	9	15,333	13	4,538
Average for all		21,026		20,672

$p \leq 0.90$

Unlike the Louisiana study (5), we found no association of an increase in disk of lung cancer among current smokers, ex-smokers, or never-smokers and material or paternal (yes/no) smoking habits.

Smoking history and histology

Among the ever-smokers, there was a predominance of squamous and small cell types of lung tumours, whereas the opposite pattern of a predominance of adenocarcinomas was found for those passively exposed and the N category (Table V). There was no significant difference in cell type distribution between the passively exposed women and those with no regular exposure. The predominance of adenocarcinomas in the never-smoked women as a group, regardless of their passive smoking history, has been reported elsewhere (1, 4, 10).

Table V - *Smoking history and histology.*

Smoking history	Cell type	
	Squamous + Small Cell	Adenocarcinoma + Large Cell
Ever smoked	64% (61/95)	36% (34/95)
Passive smoking	42% (25/59)	58% (34/59)
None	37% (7/19)	63% (12/19)

Risk among never-smokers

We have earlier shown that the average total amount of hours or years of passive smoking among the never-smokers was not significantly different between patients and controls. We also did not find a higher RR among patients with passive exposure levels of > 35,000 hours (3 hours 12 min./day x 30 years) than those with lower exposures (Table VI).

Table VI - *RR of lung cancer among never-smokers by levels of passive exposure.*

Category	Patients	Controls	RR	p value
None	22	40	1.00	
Low[1]	57	81	1.28	≤0.44
High[2]	9	16	1.02	≤0.96
Total passive	66	97	1.24	≤0.49

[1] ≤ 35,000 hours
[2] > 35,000 hours

It is possible that the bronchial mucosa is more susceptible to carcinogens before adulthood than later in life. Table VII summarized our data on age when passive exposure started for the never-smokers. There was no significant difference between patients and controls in their ages at first exposure. In fact, there were more controls who had been exposed before the age of 20 years than their matched patients. Thus our data were unable to substantiate the possibility raised by Doll and Peto (7) that « life-long exposure (including childhood) may have four times the effect of exposure which is limited to adult life ».

Table VII - *Age passive exposure started for never-smokers.*

Age	Patients		Controls	
	No.	(%)	No.	(%)
0 - 19	15	(23)	30	(31)
20 - 39	42	(64)	50	(52)
40+	9	(14)	17	(18)
Total	66		97	
Average age	34.6		34.3	

$p \leq 0.10$

Risk for ever-smokers

It is well established that not all smokers, not even heavy ones, will develop

lung cancer. To see if passive smoking adds risk to active smokers, the risks for light smokers (< 100 kg tobacco or 14 pack years) with low or no passive exposure (< 15,000 hours or 1.5 hours/day x 30 years) and those smoking similar amounts but with heavy passive smoke exposures were compared (Table VIII). The same comparison was applied also to the heavy smokers (> 100 kg or 14 pack years). We found not only no increase but an actual decrease in the risk for both light and heavy smokers with heavy passive exposure compared to those with no or low exposure. There was only an increase in the risk related to the levels of their own cigarette consumption. This result was also found by Correa et al. (5).

Table VIII - *RR for smokers with and without passive exposure.*

Type	Patients	Controls	RR
Light smokers[1] with Low[2] or no exposure	18	19	1.00
Light smokers with heavy[3] exposure	3	13	0.24
Heavy smokers[4] with low or no exposure	48	14	3.62
Heavy smokers with heavy exposure	43	17	2.67
Total	112	63	

[1] ≤ 100 kg tobacco
[2] < 15,000 hours
[3] > 100 kg tobacco
[4] ≥ 15,000 hours

Discussion

In this retrospective study on the possible influence of passive smoking on the high incidence of lung cancer in Hong Kong Chinese females, we have attempted to identify and quantify various sources and types of tobacco exposure among 200 patients and 200 district controls. We have limited our data presentation to show only those factors relevant to the issue of passive smoking. A more detailed description and discussion of active smoking as a risk factor was presented elsewhere (15).

The apparent lack of an association between passive smoking and the risk of lung cancer in our study may be due to possibilities which occur because passive smoking may be only a very weak carcinogen, whose effect may be concealed by other factors that play a role in a multifactorial and multistage aetiology. Among the female never-smokers, intervening factors might cause an overshadowing or a protective effect (e.g. bronchial irritation, dietary nitrosamines or beta-carotene). These factors in Hong Kong are likely to be different from those in Japan (12), U.S.A. (9, 16), or Greece (17, 18), and this difference may explain our different results. The possibility that the « dose-response curve resembles a logistic in shape » such that « there is a dose greater than zero which produces zero response » was considered by Hammond and Selikoff (11) and may be operating here.

Certainly the lack of an increased risk for the active smokers from passive smoking, which was also found by Correa et al. (5). Would seem to support the possibility that the effects of active smoking or, indeed, other factors yet to be identified, greatly overshadowed the carcinogenic action of passive smoking.

This, however, does not imply that passive smoking is innocuous, as it may contribute an added risk of other respiratory, and cardiovascular diseases (8, 14, 16). The possibility of other factors like diet, previous history of respiratory diseases, occupational exposures, use of inhalants, etc., overshadowing or inhibiting the effects of passive smoking on the risk of lung cancer among never-smoked females in Hong Kong and also the roles of these factors in the carcinogenesis are being investigated.

It is hoped that more direct assessment of passive smoking by other workers in other areas can shed more light on the passive smoking controversy.

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